### (19) World Intellectual Property Organization International Bureau





#### (43) International Publication Date 1 March 2001 (01.03.2001)

## PCT

# (10) International Publication Number WO 01/14365 A1

(51) International Patent Classification7: C07D 321/00. A61K 31/335

David, M. [US/US]; 2817 32nd Avenue South, Seattle, WA 98144 (US). SIMON, Julian, A. [US/US]; 5300 S. Hudson, Seattle, WA 98118 (US). TZUNG, Shie-Pon [CN/US]; 23808 SE 44th Ct., Issaquah, WA 98029 (US).

(21) International Application Number: PCT/US00/22891

> (74) Agents: SANDBAKEN, Mark, G. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111-3834 (US).

(22) International Filing Date: 18 August 2000 (18.08.2000)

(81) Designated States (national): AU, CA, JP, US.

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/149,968 20 August 1999 (20.08.1999) (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(71) Applicant (for all designated States except US): FRED HUTCHINSON CANCER RESEARCH CENTER [US/US]; 1100 Fairview Avenue N., M/S: C2M 027, Seattle, WA 98109-1024 (US).

#### Published:

With international search report.

(72) Inventors; and

(75) Inventors/Applicants (for US only): HOCKENBERY,

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



(54) Title: COMPOSITIONS AND METHODS FOR MODULATING APOPTOSIS IN CELLS OVER-EXPRESSING bc1-2 FAM-ILY MEMBER PROTEINS

(57) Abstract: The present invention provides agents and compositions for modulating the apoptotic state of a cell. The agents comprise derivatives of antimycins which bind to an anti-apoptotic Bcl-2 family member protein. Further, the agents preferentially induce apoptosis in cells that over-express anti-apoptotic Bcl-2 family member proteins and typically exhibit reduced binding affinity for cytochrome B. Pharmaceutical uses of the agents and compositions include treating apoptosis-associated disease, such as neoplasia and drug resistance, are also disclosed.